

COOLWATER TRIM™ 75 DAY PRE-MARKET NOTIFICATION

APPENDIX C: MECHANISMS OF ACTION

Overview

In this Appendix there are 3 articles. These articles provide a basic understanding of the mechanism of how HCA works.

The first article is by John Lowenstein of Brandeis University who was one of the key figures in the early research conducted on HCA. The article entitled "Experiments with Hydroxycitrate" is an overview of much of his work. His important conclusion is that the citrate cleavage pathway is the major source of carbon for the synthesis of fatty acid in rat. Proving that hypothesis was made possible by using the knowledge that (-)-hydroxycitrate is an inhibitor of citrate cleavage enzyme.

The second article entitled "Tricarballylate and Hydroxycitrate: Substrate and Inhibitor of ATP: Citrate Oxaloacetate Lyase" is an investigation into the activity of the citrate cleavage enzyme. The study was also conducted by Lowenstein and his colleagues at Brandeis University. It provides evidence that the (-)-isomer of hydroxycitrate is indeed an inhibitor of citrate cleavage enzyme

The third study presented in this Appendix was led by Harry Preuss of Georgetown University Medical Centre and is an investigation of the effects of a natural extract of (-)-hydroxycitric acid alone and in combination with other natural ingredients on weight loss. The study was conducted under controlled circumstances on 60 moderately obese subjects. The findings after 8 weeks of HCA supplementation were that appetite, Body Mass Index, total cholesterol, low-density lipoproteins, triglycerides and serum leptin levels were significantly reduced, while high density lipoprotein levels and excretion of urinary fat metabolites had increased. In effect, HCA was shown to be a useful aid in a diet regime while it also contributed to healthy blood lipid profiles.

These three articles are representative of many other studies that have been conducted on the effects of HCA.

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Tricarballylate And Hydroxycitrate: Substrate And Inhibitor Of Atp Citrate Oxaloacetate Lyase John A Watson, Marie Fang and John M Lowenstein

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Effects of a natural extract of (--)-hydroxycitric acid (HCA-SX) and a combination of HCA-SX plus niacin-bound chromium and Gymnema sylvestre extract on weight loss H. G. Preuss, 1 D. Bagchi, 2 M. Bagchi, 2 C. V. S. Rao, 3 D. K. Dey 4 and S. Satyanarayana 51